

FIGURE 1

09913667 072701

Cleave tags

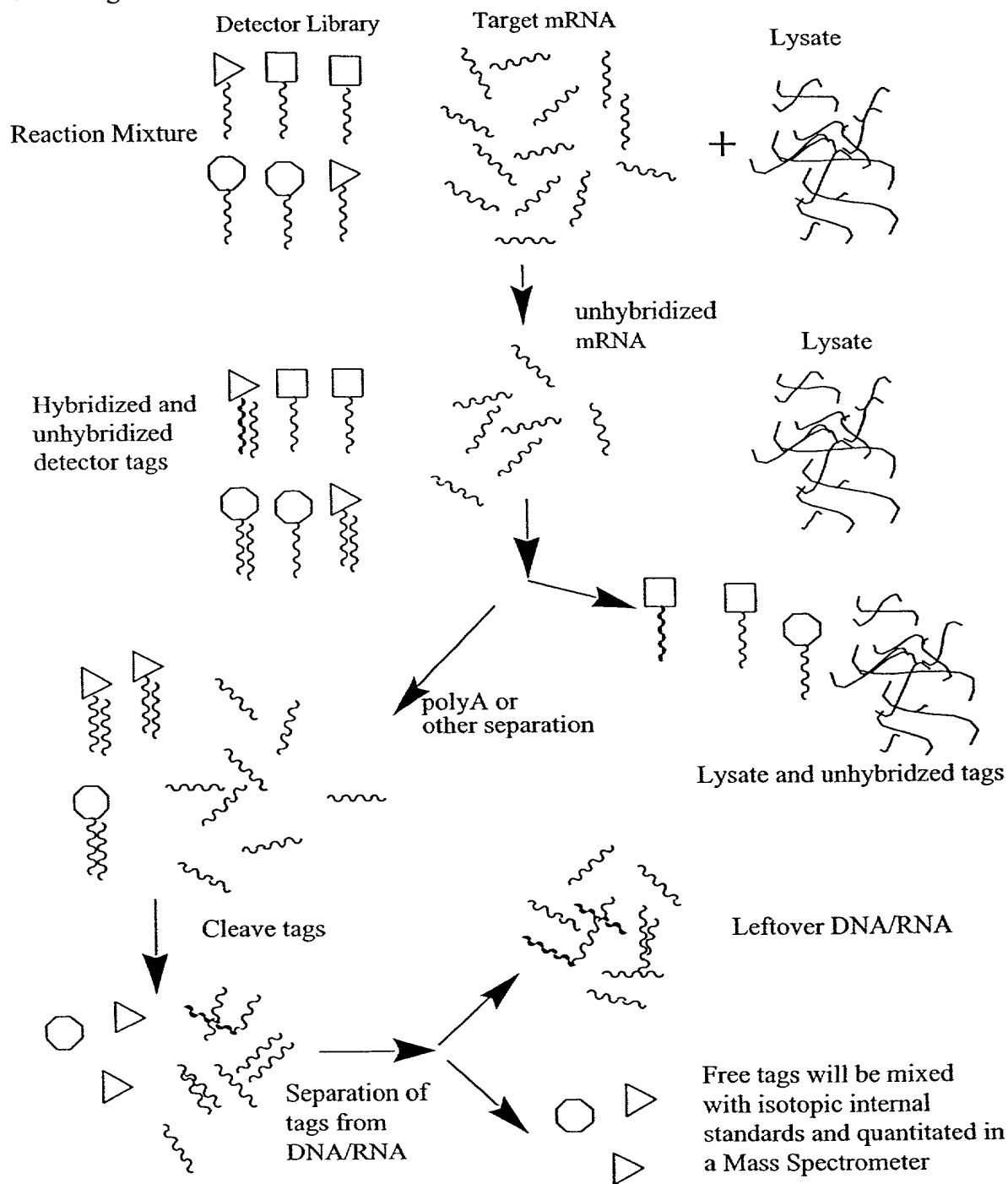


FIGURE 2

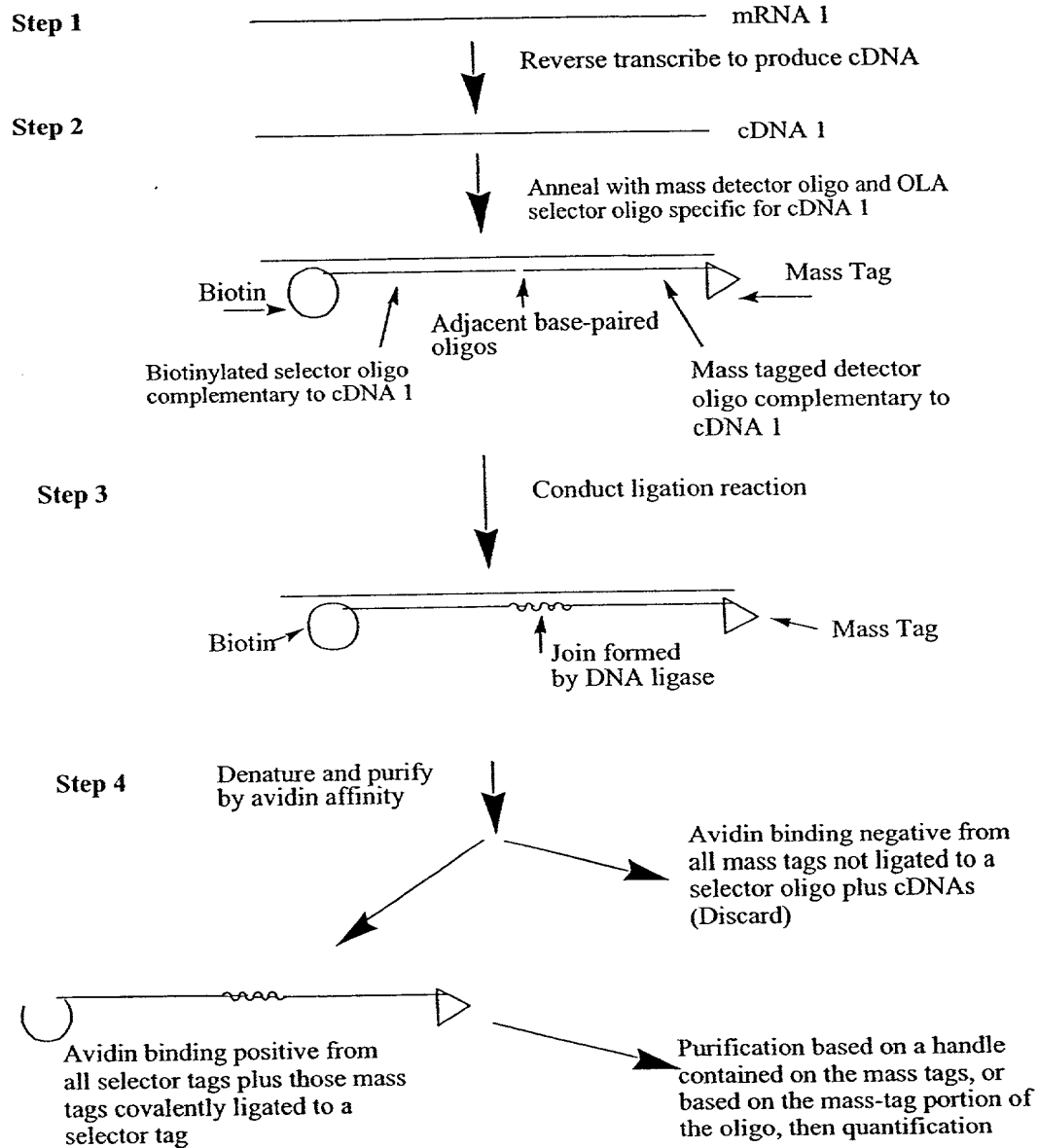


FIGURE 3

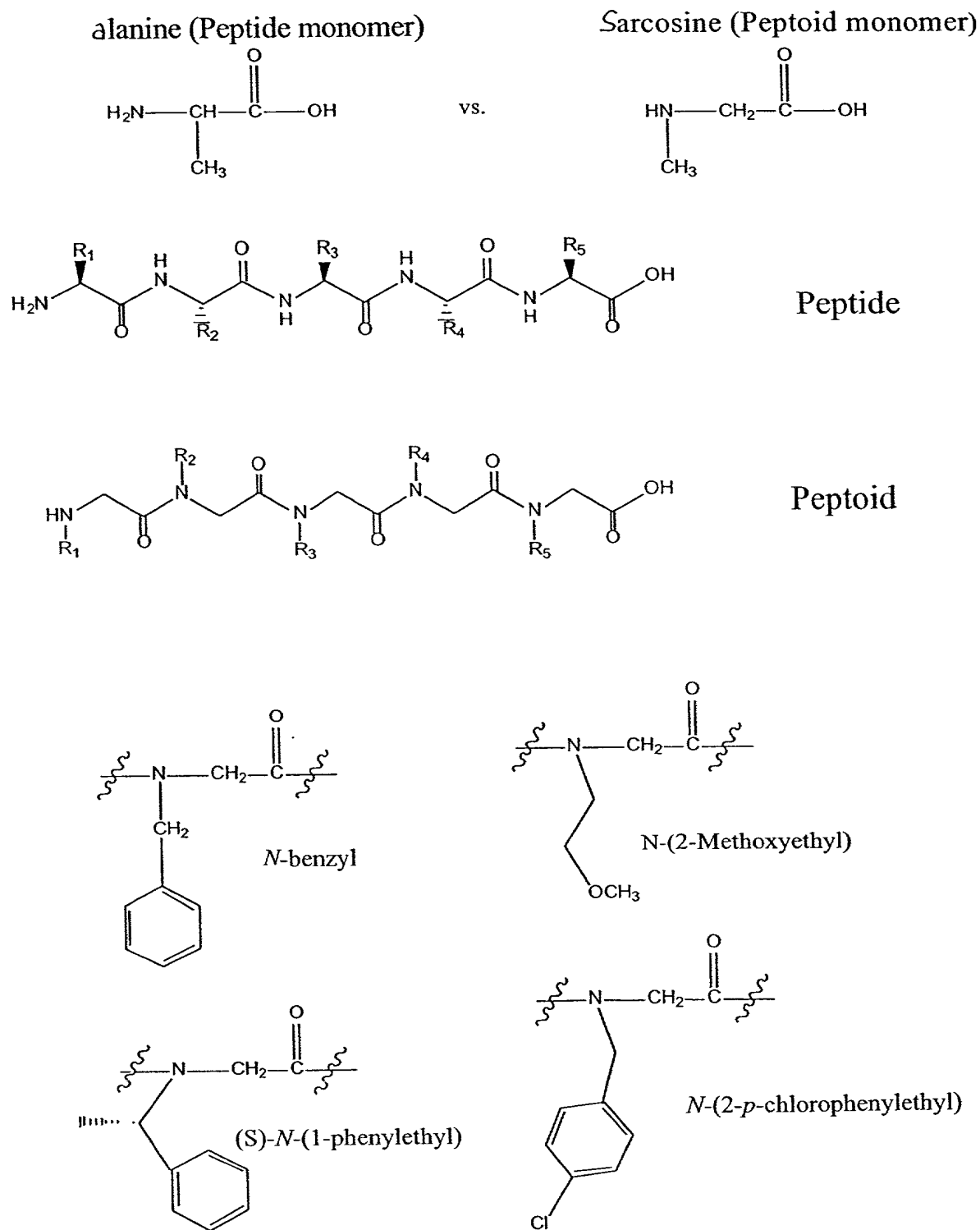


FIGURE 4

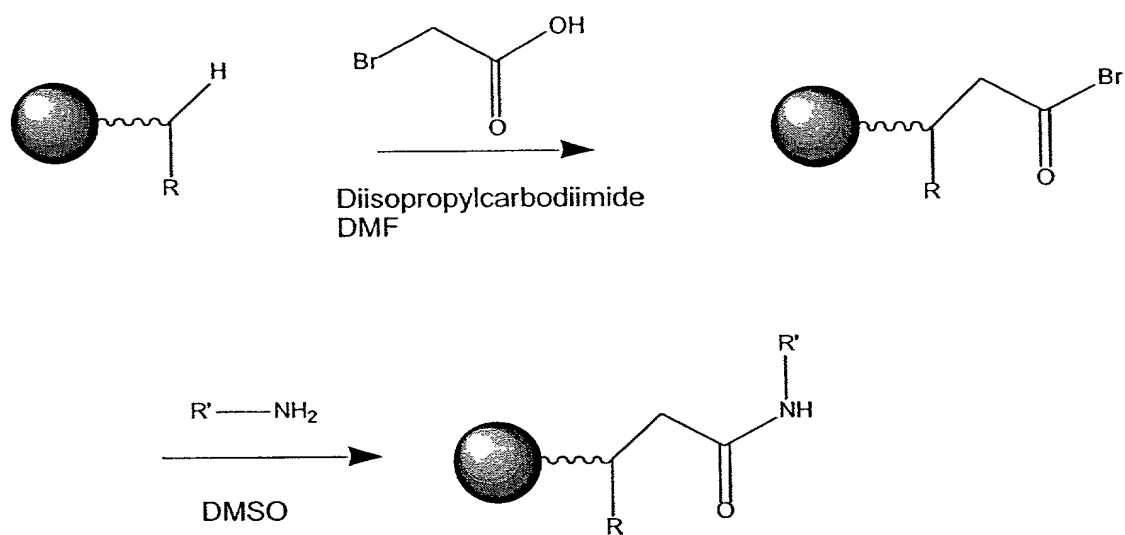
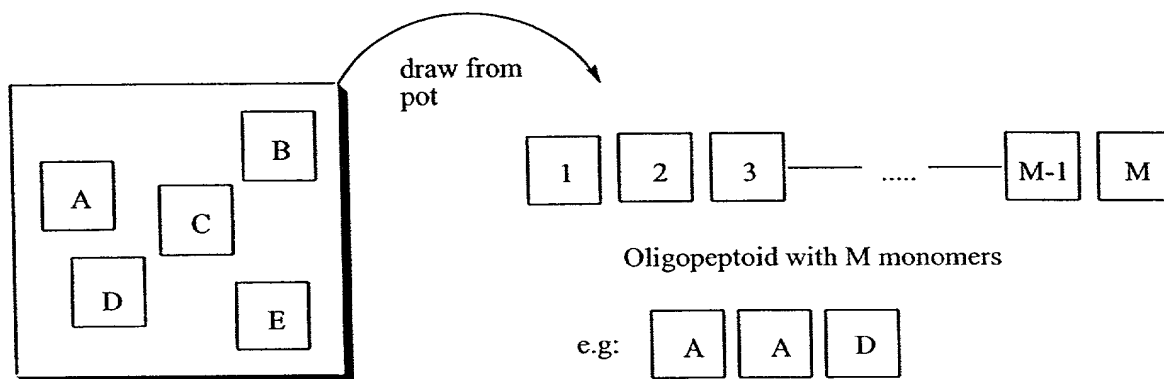


FIGURE 5

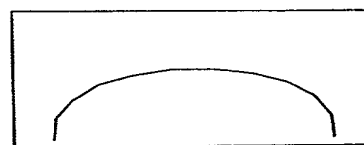


N monomers of unique mass

L = # of different peptoids with a unique combination of monomers

$$L = \binom{M+N-1}{N}$$

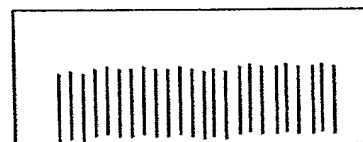
Example: 10 monomers, hexamer peptoids, yields 5005 combinations, or 8007 if pentamers and fewer are used too.



Mostly uniform distribution of molecular weights

Process library by removing coincidental combinations, when two unique combinations have the same mass

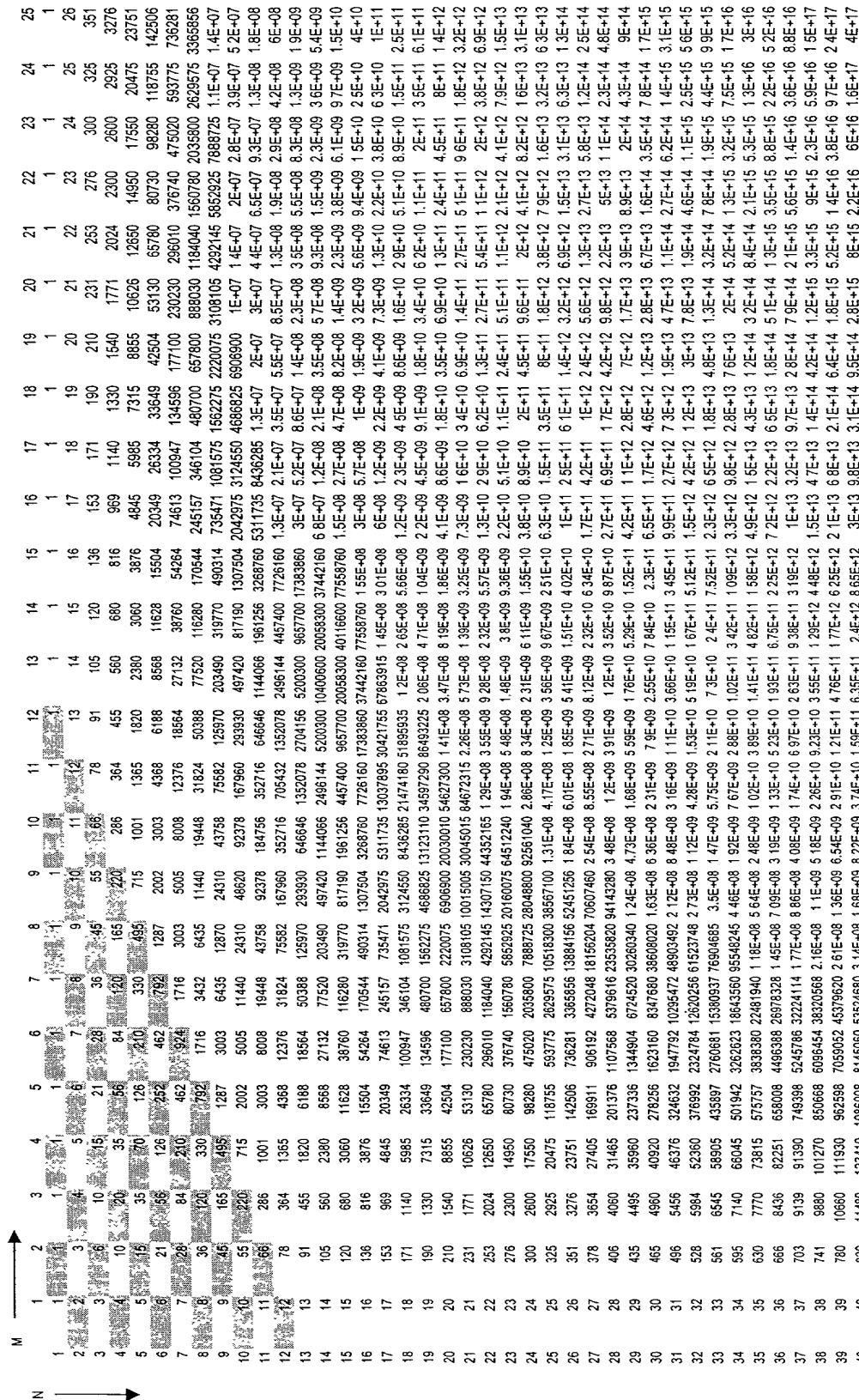
Also enforce other requirements, such as a minimum of X Daltons between species, or structural requirements such as at least two charged bases.



Desirable distribution of molecular weights

Assign oligo probes to tags and log, output library structure to peptoid synthesizer

FIGURE 6



M=length of polypeptoid
N=# of monomers of unique mass

Figure 8A

N	M												
		1	2	3	4	5	6	7	8	9	10	11	12
1	1	1	2	3	4	5	1	6	7	8	9	1	10
2	2	2	5	9	14	20	27	35	44	54	65	77	90
3	3	3	9	19	34	55	83	119	164	219	285	363	454
4	4	4	14	34	69	125	209	329	494	714	1000	1364	1819
5	5	5	20	55	125	251	461	791	1286	2001	3002	4367	6187
6	6	6	27	83	209	461	923	1715	3002	5004	8007	12375	18563
7	7	7	35	119	329	791	1715	3431	6434	11439	19447	31823	50387
8	8	8	44	164	494	1286	3002	6434	12869	24309	43757	75581	125969
9	9	9	54	219	714	2001	5004	11439	24309	48619	92377	167959	293929
10	10	10	65	285	1000	3002	8007	19447	43757	92377	184755	352715	646645
11	11	11	77	363	1364	4367	12375	31823	75581	167959	352715	705431	1352077
12	12	12	90	454	1819	6187	18563	50387	125969	293929	646645	1352077	2704155
13	13	13	104	559	2379	8567	27131	77519	203489	497419	1144065	2496143	5200299
14	14	14	119	679	3059	11627	38759	116279	319769	817189	1961255	4457399	9657699
15	15	15	135	815	3875	15503	54263	170543	490313	1307503	3268759	7726159	17383859
16	16	16	152	968	4844	20348	74612	245156	735470	2042974	5311734	13037894	30421754
17	17	17	170	1139	5984	26333	100946	346103	1081574	3124549	8436284	21474179	51895934
18	18	18	189	1329	7314	33648	134595	480699	1562274	4686824	13123109	34597289	86493224
19	19	19	209	1539	8854	42503	177099	657799	2220074	6906899	20030009	54627299	141120524
20	20	20	230	1770	10625	53129	230229	888029	3108104	10015004	30045014	84672314	225792839
21	21	21	252	2023	12649	65779	296009	1184039	4292144	14307149	44352164	129024479	354817319
22	22	22	275	2299	14949	80729	376739	1560779	5852924	20160074	64512239	193536719	548354039
23	23	23	299	2599	17549	98279	475019	2035799	7888724	28048799	92561039	286097759	834451799
24	24	24	324	2924	20474	118754	593774	2629574	10518299	38567099	131128139	417223899	1251677699
25	25	25	350	3275	23750	142505	736280	3365855	13884155	52451255	183579395	600805295	1852482995
26	26	26	377	3653	27404	169910	906191	4272047	18156203	70607459	254186855	854992151	2707475147
27	27	27	405	4059	31464	201375	1107567	5379615	23535819	94143279	348330135	1203322287	3910797435
28	28	28	434	4494	35959	237335	1344903	6724519	30260339	124403619	472733755	1676056043	5586853479
29	29	29	464	4959	40919	278255	1623159	8347679	38608019	163011639	635745395	2311801439	7898654919
30	30	30	495	5455	46375	324631	1947791	10295471	48903491	211915131	847660527	3159461967	11058116887
31	31	31	527	5983	52359	376991	2324783	12620255	61523747	273438879	1121099407	4280561375	15338678263
32	32	32	560	6544	58904	435896	2760680	15380936	76904684	350343564	1471442972	5752004348	21090682612
33	33	33	594	7139	66044	501941	3262622	18643559	95548244	445891809	1917334782	7669339131	28760021744
34	34	34	629	7769	73814	575756	3838379	22481939	118030184	563921994	2481256777	10150595909	38910617654
35	35	35	665	8435	82250	658007	4496387	26978327	145008512	708930507	3190187285	13340783195	52251400850
36	36	36	702	9138	749397	5245785	32224113	177232626	886163134	4076350420	17417133616	22595200367	92263734835
37	37	37	740	9879	101269	850667	6096453	38320567	21553194	1101716329	5178066750	22595200367	92263734835
38	38	38	779	10659	111929	962597	7059051	45379619	260932814	1362649144	6540715895	29135916263	1.21E+11
39	39	39	819	11479	123409	1086007	8145059	53524679	314457494	1677106639	8217822535	37353738799	1.59E+11
40	40	40	860	12340	135750	1221758	9366818	62891498	377348993	2054455633	10272278169	47626016969	2.06E+11

→

N	M	→											
		13	14	15	16	17	18	19	20	21	22	23	24
1	1	11	12	13	1	14	15	16	17	1	18	19	20
2	2	104	119	135	152	170	189	209	230	252	275	299	324
3	3	559	679	815	968	1139	1329	1539	1770	2023	2299	2599	2924
4	4	2379	3039	3875	4844	5984	7314	8854	10625	12649	14949	17549	20474
5	5	8567	11627	15503	20348	26333	33648	42503	53129	65779	80729	98279	118754
6	6	27131	38759	54263	74612	100946	134595	177099	230229	296009	376739	475019	593774
7	7	77519	116279	170543	245156	346103	480699	657799	888029	1184009	1560779	2035799	2629574
8	8	203489	319769	490313	735470	1081574	1562274	2220074	3108104	4292144	5852924	7886724	10518239
9	9	497419	817189	1307503	2042974	3124549	4686824	6906899	10015004	14307149	20160074	28048799	38567099
10	10	1144065	1961255	3268759	5311734	8436284	13123109	20030009	30045014	44352164	64512239	92561039	131128139
11	11	5200239	9657699	17383859	30421754	51895934	86493224	141120524	225792839	354817319	548354039	835451799	1251677699
12	12	10400599	20058239	37442159	67863914	119759849	206253074	347373599	573166439	927983759	1476337799	2310789599	3562467299
13	13	20058299	40116599	77558759	145422674	265182524	437158319	7307872109	12875774669	22239974429	37711260989	58732378799	88732378799
14	14	37442159	77558759	145422674	265182524	437158319	7307872109	12875774669	22239974429	37711260989	58732378799	88732378799	130377E+11
15	15	7863914	145422674	265182524	437158319	7307872109	12875774669	22239974429	37711260989	58732378799	88732378799	130377E+11	254682E+11
16	16	119759849	265182524	437158319	7307872109	12875774669	22239974429	37711260989	58732378799	88732378799	130377E+11	254682E+11	608359E+11
17	17	206253074	437158319	7307872109	12875774669	22239974429	37711260989	58732378799	88732378799	130377E+11	254682E+11	608359E+11	140893E+12
18	18	347373599	81809199	1855967519	405928949	8597496599	17672631899	35345263799	68923264409	131282E+11	244663E+11	446775E+11	800472E+11
19	19	573166439	1391975639	3247943159	7307872109	1590368709	33578000609	68923264409	131282E+11	244663E+11	446775E+11	800472E+11	140893E+12
20	20	927983759	2319959399	5567902559	12875774669	28781143379	62359143989	131282E+11	244663E+11	446775E+11	800472E+11	140893E+12	316987E+12
21	21	1476337799	3796297199	9364199759	22239974429	51021117809	11338E+11	244663E+11	446775E+11	800472E+11	140893E+12	316987E+12	694353E+12
22	22	3796297199	9364199759	22239974429	51021117809	11338E+11	244663E+11	446775E+11	800472E+11	140893E+12	316987E+12	694353E+12	126411E+14
23	23	3562467299	9669554099	25140840659	62852101649	151584E+11	33697E+11	800472E+11	176104E+12	377366E+12	789037E+12	161238E+13	322476E+13
24	24	5414950295	15084504395	40225345055	103077E+11	254662E+11	608359E+11	140893E+12	316987E+12	694353E+12	148339E+13	309577E+13	632053E+13
25	25	8122425443	23206929839	63432274895	16651E+11	421172E+11	102953E+12	243836E+12	560823E+12	125518E+13	273857E+13	583434E+13	121549E+14
26	26	1203222879	35240152719	98672427615	265182E+11	686354E+11	171588E+12	415425E+12	976248E+12	223142E+13	496999E+13	108043E+14	229592E+14
27	27	7620076359	52860229079	151533E+11	416715E+11	110307E+12	281895E+12	69732E+12	167357E+13	390499E+13	867498E+13	196793E+14	426385E+14
28	28	26518731279	78378960359	229912E+11	646626E+11	17497E+12	45886E+12	115418E+13	282775E+13	673274E+13	15607E+14	35287E+14	79255E+14
29	29	36576848167	114965E+11	344867E+11	991494E+11	274119E+12	73094E+12	188517E+13	471292E+13	114457E+14	270534E+14	623404E+14	179256E+15
30	30	51915526431	168871E+11	511739E+11	150323E+11	424442E+12	115543E+13	304059E+13	775392E+13	191992E+14	462528E+14	108593E+15	24859E+15
31	31	73006209044	238878E+11	751618E+11	225485E+12	649927E+12	180535E+13	484595E+13	125995E+14	317986E+14	780512E+14	186644E+15	35503E+15
32	32	101768E+11	341644E+11	109328E+12	334811E+12	994738E+12	279009E+13	763604E+13	202355E+14	520341E+14	130085E+15	31673E+15	75233E+15
33	33	140677E+11	482321E+11	157558E+12	492689E+12	147711E+13	42672E+13	119032E+14	321387E+14	841729E+14	21269E+15	53098E+15	128322E+16
34	34	192929E+11	675249E+11	225083E+12	717452E+12	219456E+13	646176E+13	18366E+14	505037E+14	134677E+15	348935E+15	879923E+15	216314E+16
35	35	262597E+11	937846E+11	318668E+12	103632E+13	323088E+13	896263E+13	240576E+14	786514E+14	213238E+15	562173E+15	14421E+16	63624E+16
36	36	354861E+11	129271E+12	448139E+12	148446E+13	471534E+13	14408E+14	424656E+14	121027E+15	334255E+15	896438E+15	233853E+16	594377E+16
37	37	47620E+11	176897E+12	625035E+12	210949E+13	682483E+13	212328E+14	636984E+14	184725E+15	51899E+15	141543E+16	375396E+16	969773E+16
38	38	63501E+11	240398E+12	865433E+12	297483E+13	979975E+13	310328E+14	947309E+14	279459E+15	798447E+15	221387E+16	596784E+16	156556E+17
39	39	841393E+11	324537E+12	118997E+13	41649E+13	139646E+14	449972E+14	139728E+15	419184E+15	121763E+16	343151E+16	93934E+16	250649E+17
40	40												

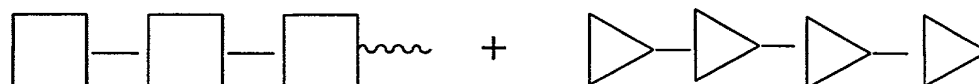
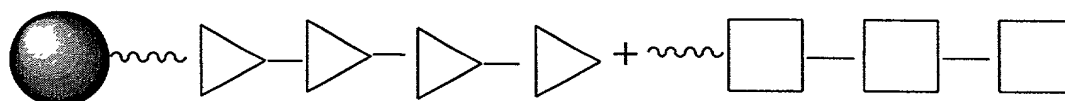
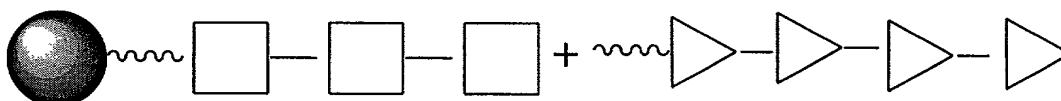
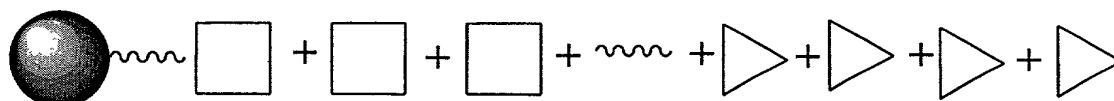
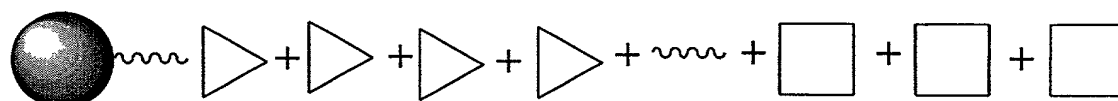
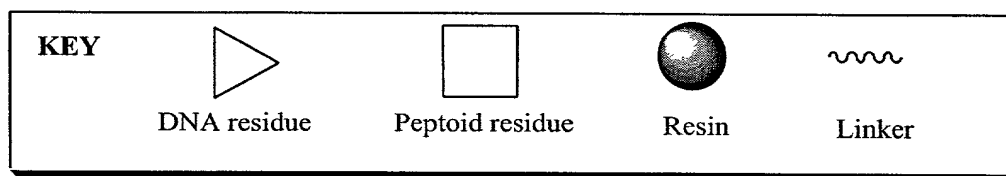


FIGURE 9

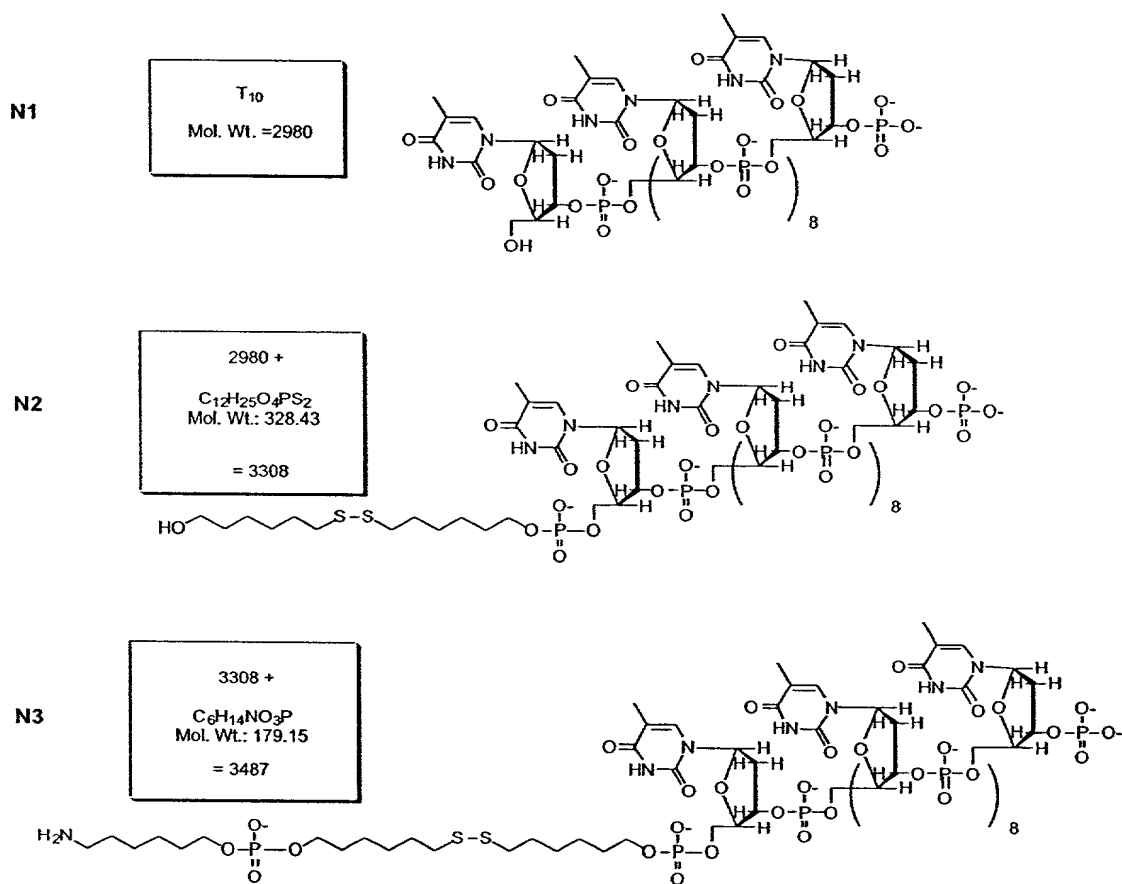


FIGURE 10

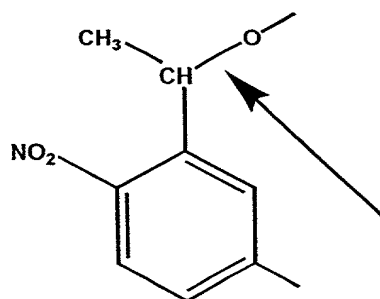


FIGURE 11A

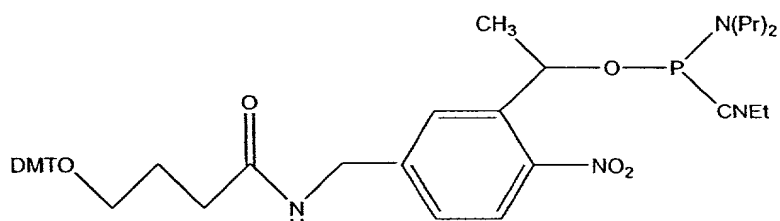


FIGURE 11B

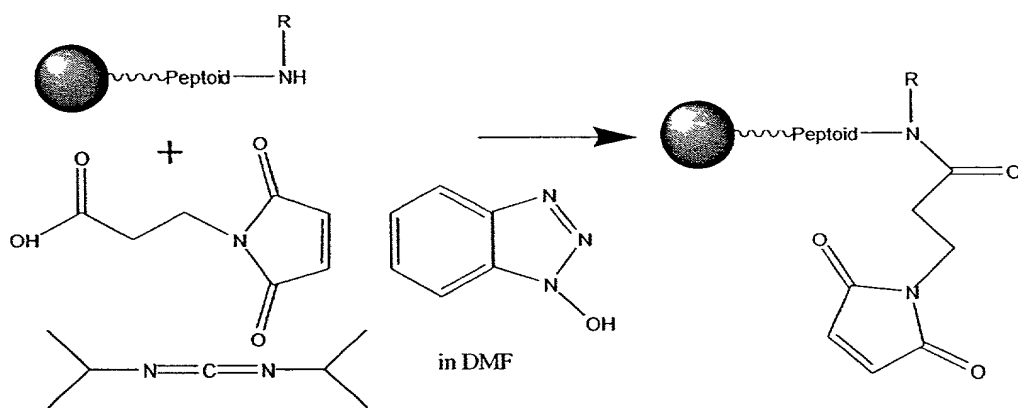
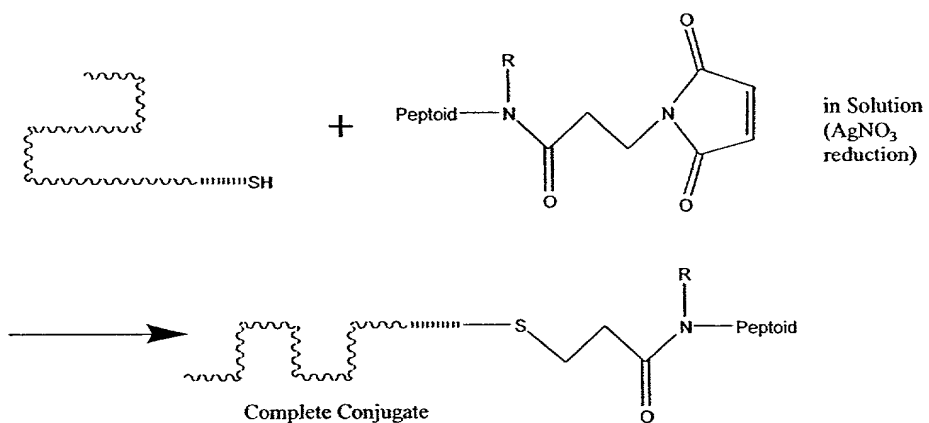


FIGURE 11C



Complete Conjugate

FIGURE 11D

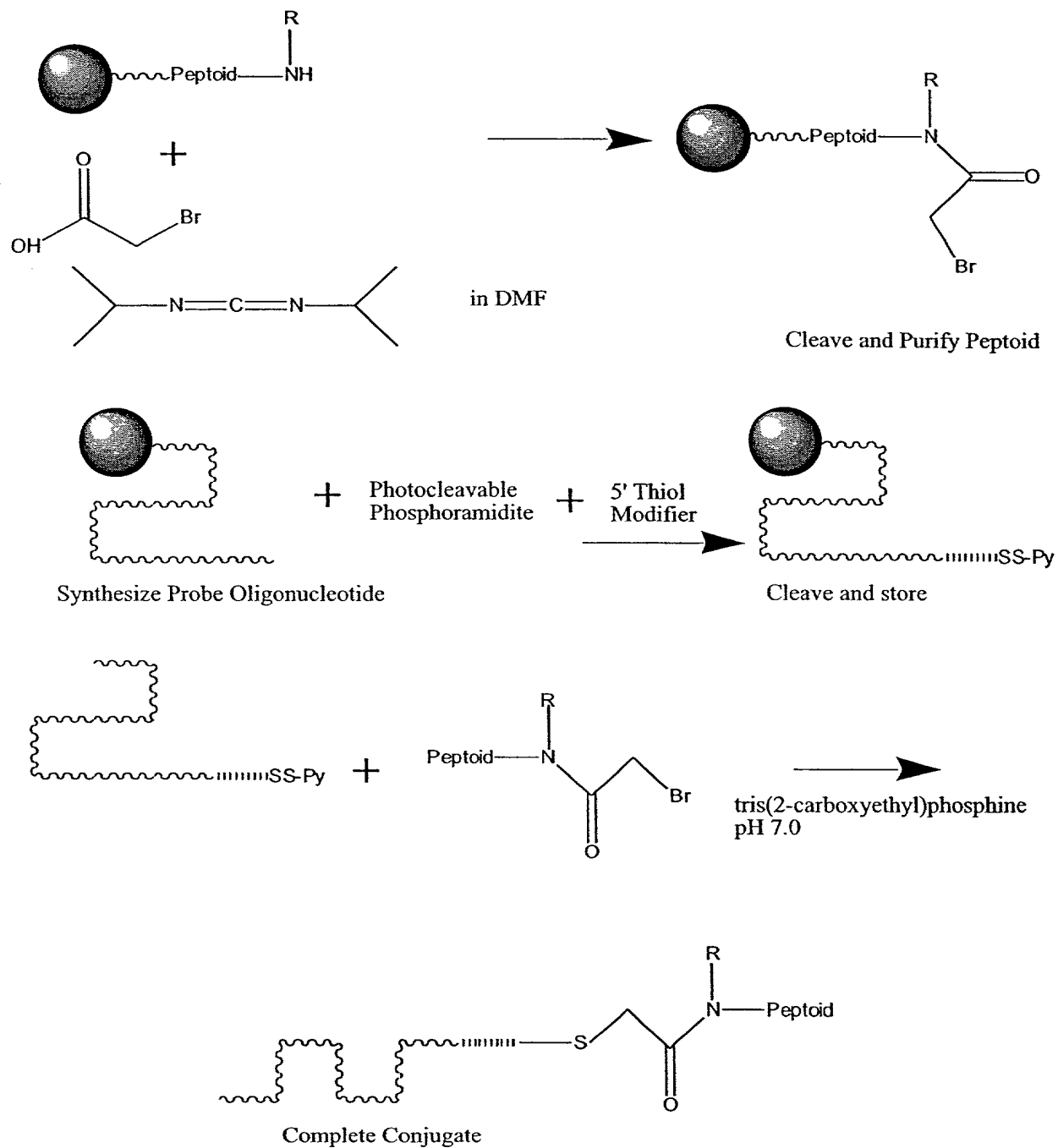
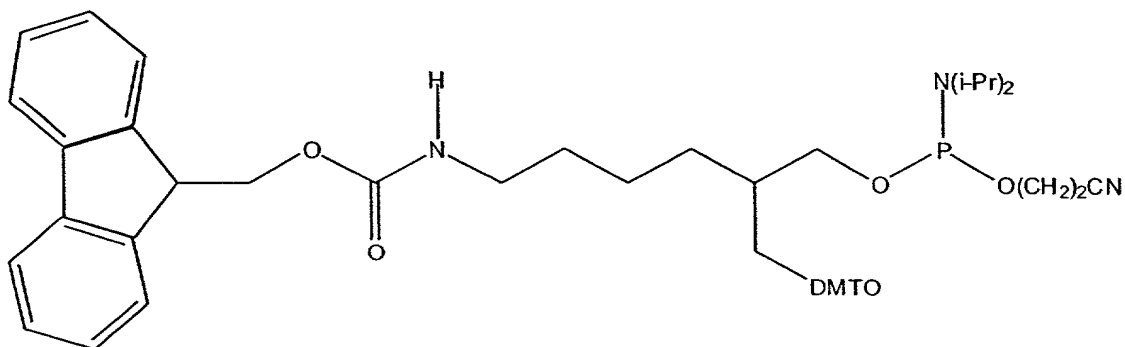


FIGURE 11E



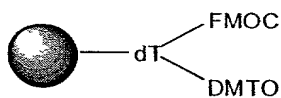
Clontech "Uni-Link AminoModifier" Branched Phosphoramidite

Method

1. Obtain Oligonucleotide Resin with dT base



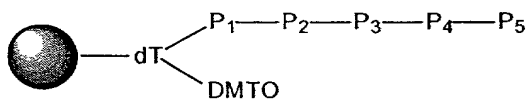
2. Add Branched Phosphoramidite



3. Transfer to Peptoid Synthesizer

4. Deprotect Fmoc

5. Add Peptoid



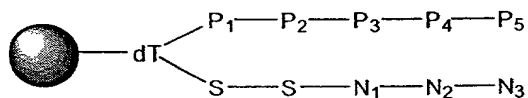
6. Protect Terminus

7. Return to ODN Synthesizer

8. Deprotect DMTO

9. Add cleavable units (Disulfide or Photocleavable)

10. Synthesize ODN



11. Deprotect and Cleave Completed Unit

FIGURE 12

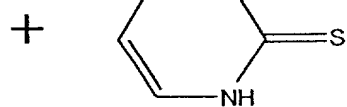
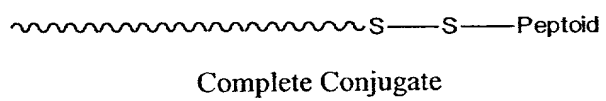
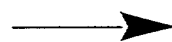
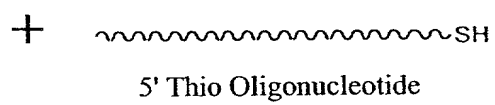
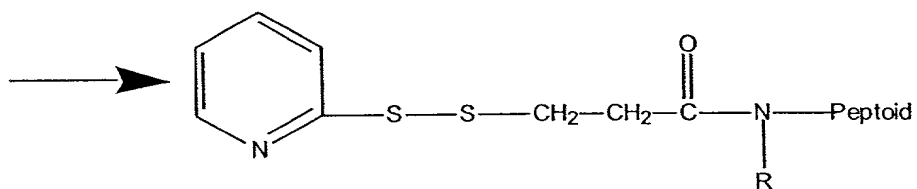
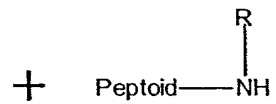
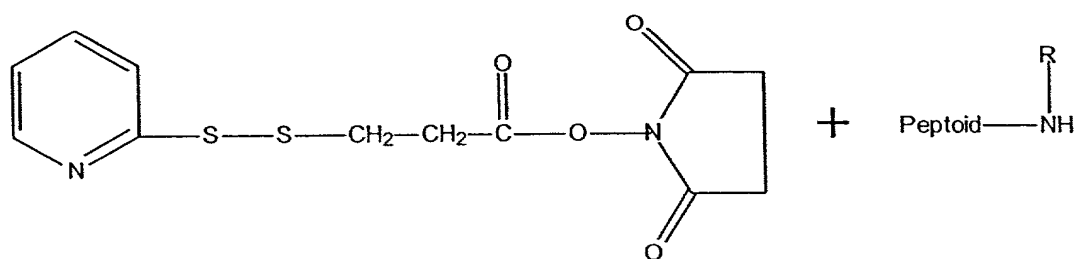


FIGURE 13

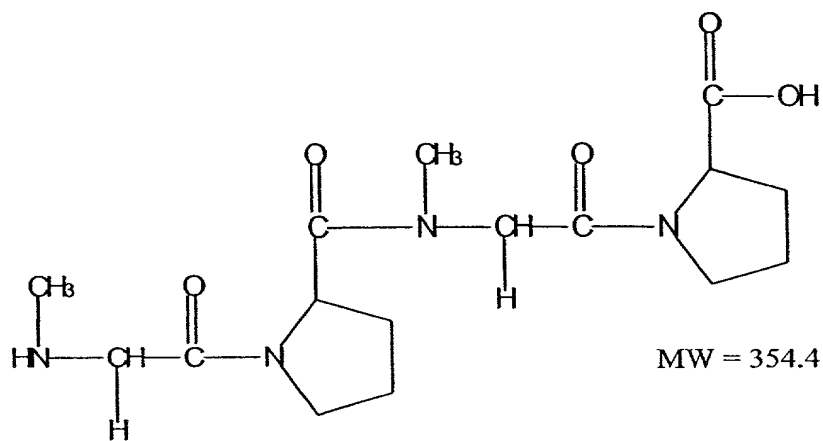


FIGURE 14

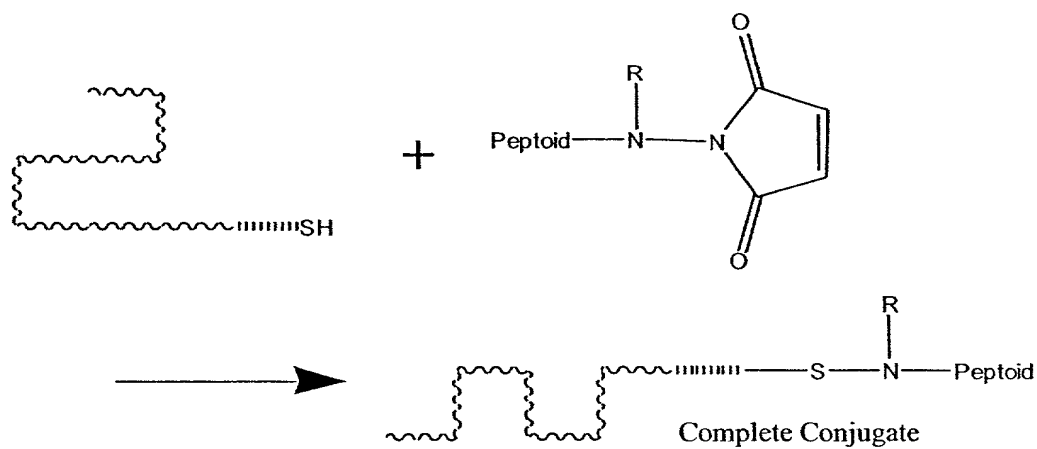
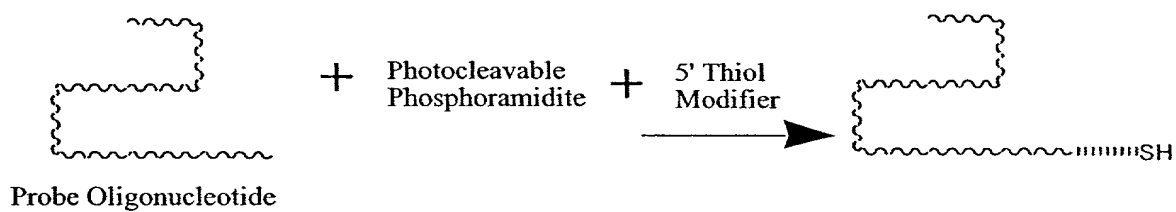
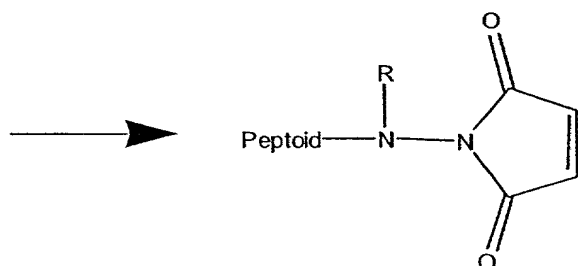
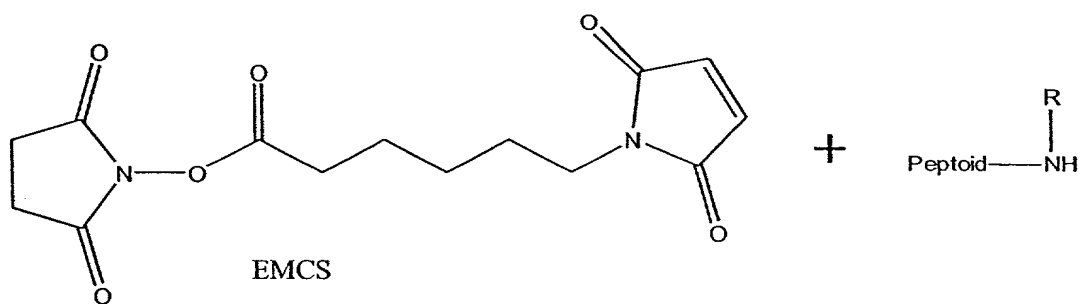


FIGURE 15

10/2/07 09:16:59

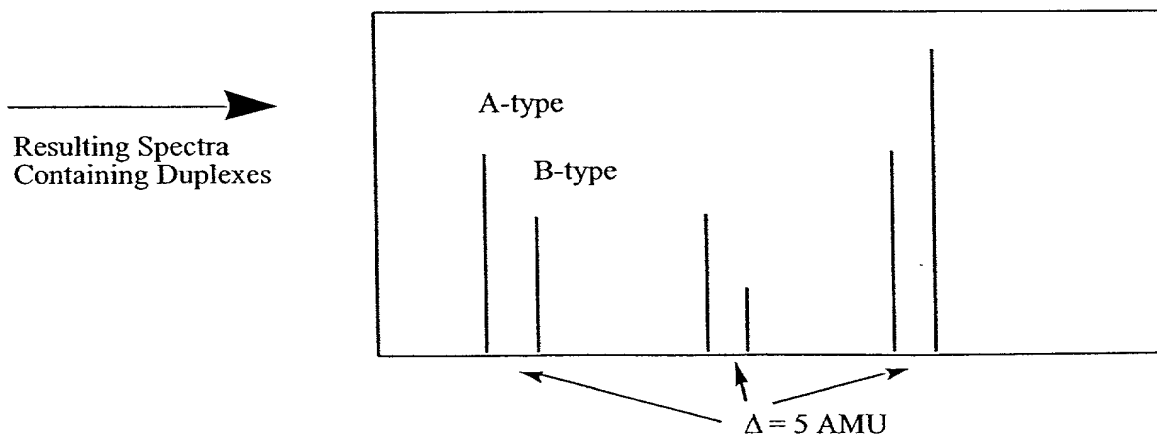
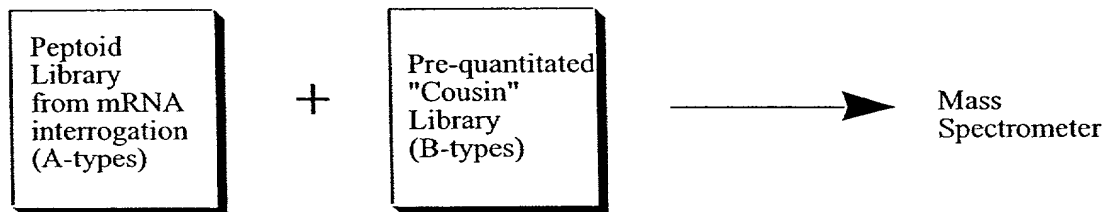
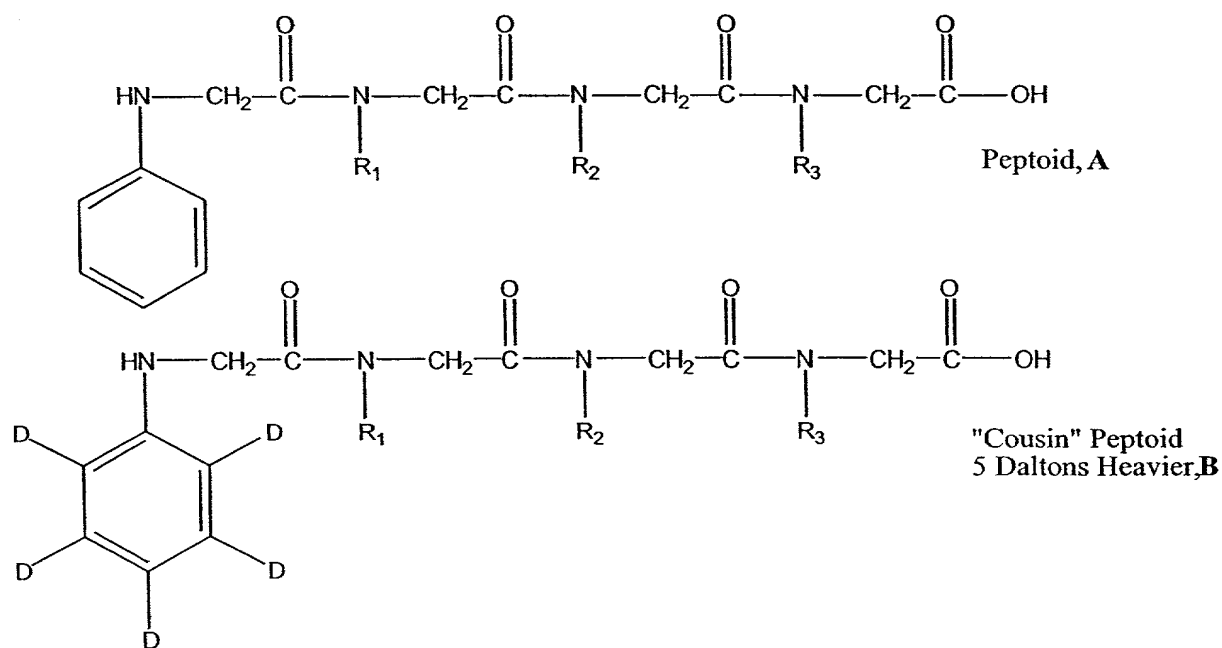


FIGURE 16

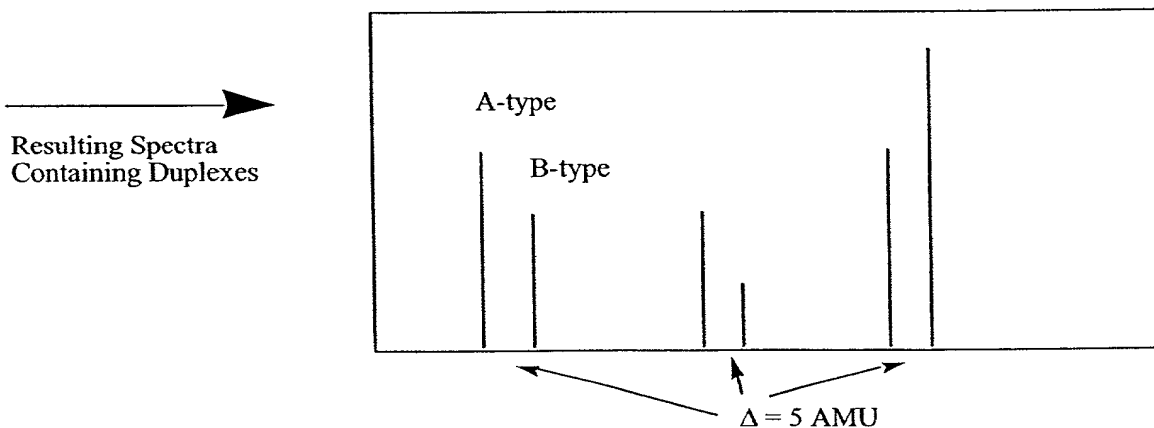
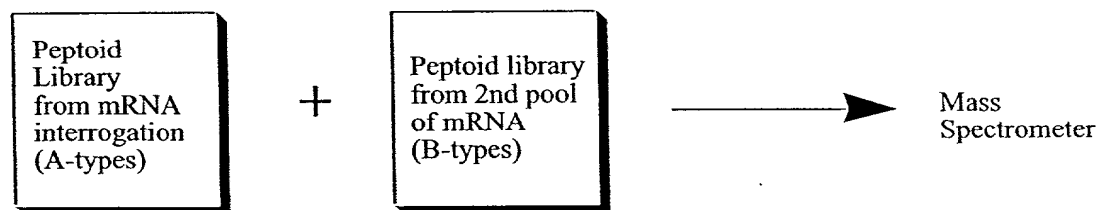
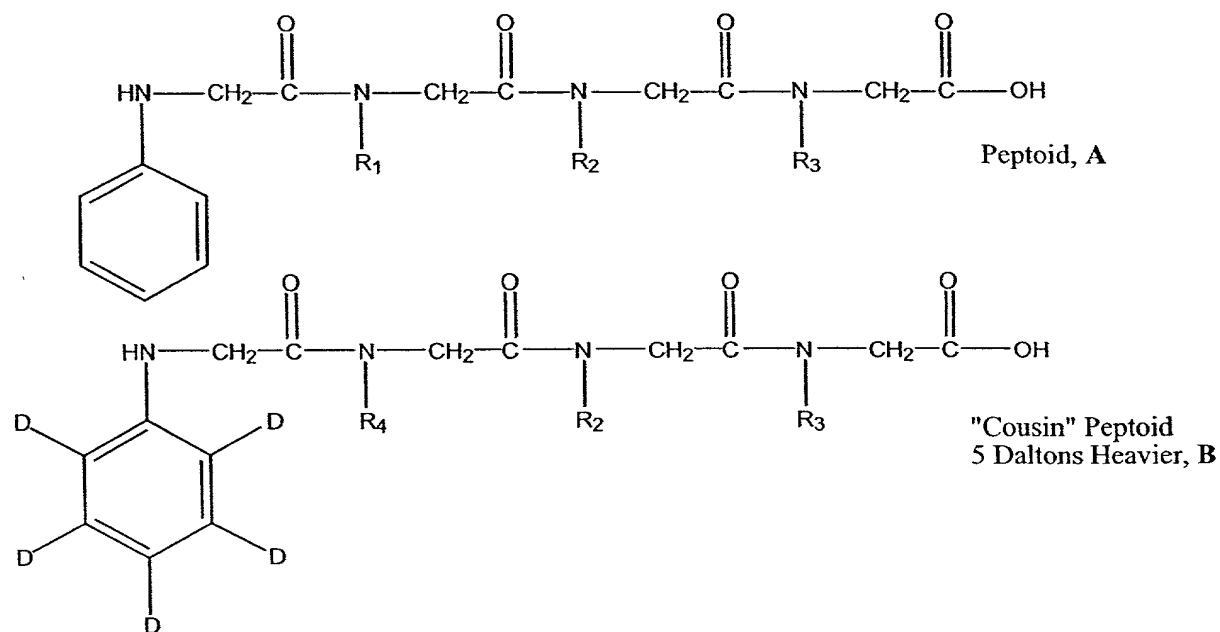


FIGURE 17

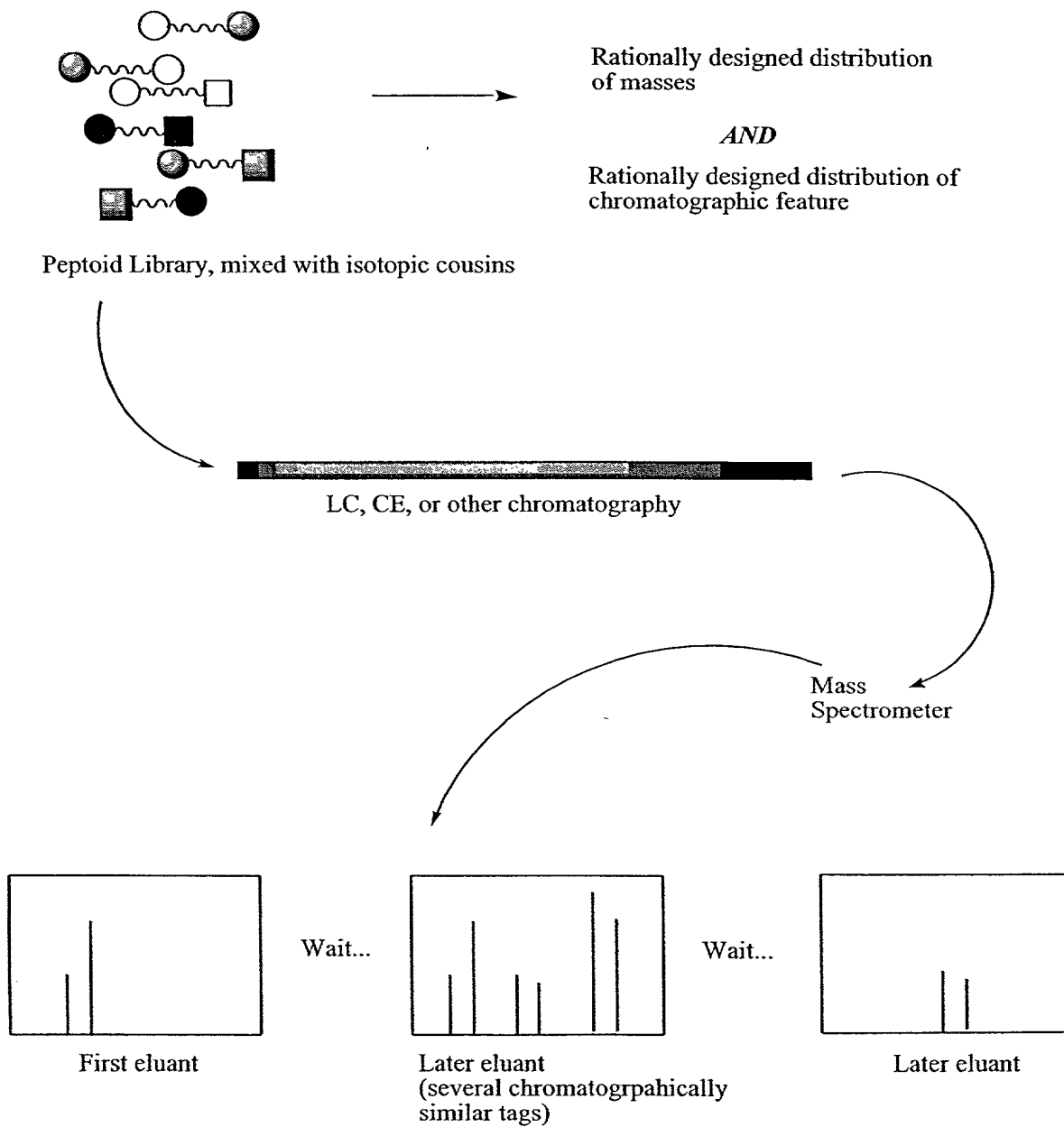
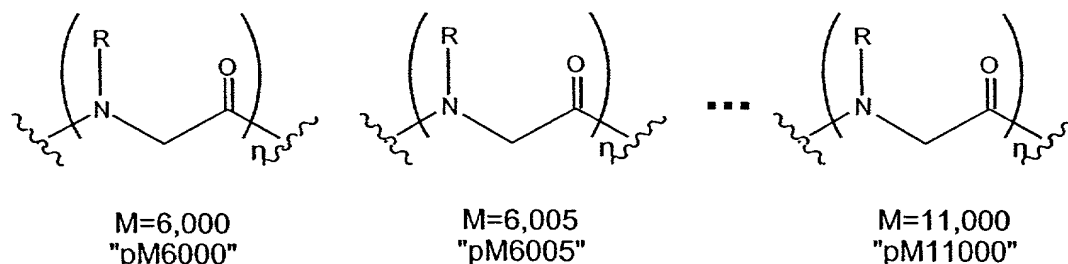


FIGURE 18

1) Synthesize and purify 1000 different peptoid oligomer mass tags, of mass 6,000 to 11,000 Daltons.



This will be performed by a robotic synthesizer on solid phase, with oligomer lengths of up to 40 residues. Molecular weights per residue will be 150-300 Daltons.

2) Synthesize and purify 16,000 different DNA oligos, complementary to the mRNA specie to be detected. Create 16 libraries of 1,000 oligos each.

AA(NNNNNNNN)₁, AA(NNNNNNNN)₂, ..., AA(NNNNNNNN)_{1,000}

AC(NNNNNNNN)₁, AC(NNNNNNNN)₂, ..., AC(NNNNNNNN)_{1,000}

.....

TT(NNNNNNNN)₁, TT(NNNNNNNN)₂, ..., TT(NNNNNNNN)_{1,000}

3) Specifically conjugate oligos in each library to a corresponding peptoid mass tag.

AA(NNNNNNNN)₁/pM6000, AA(NNNNNNNN)₂/pM6005, ..., AA(NNNNNNNN)_{1,000}/pM11000

AC(NNNNNNNN)₁/pM6000, AC(NNNNNNNN)₂/pM6005, ..., AC(NNNNNNNN)_{1,000}/pM11000

.....

TT(NNNNNNNN)₁/pM6000, TT(NNNNNNNN)₂/pM6005, ..., TT(NNNNNNNN)_{1,000}/pM11000

4) Purify DNA/peptoid mass tag products and combine library elements into 16 pools.

FIGURE 19

Mass-tagging on a chip: How to measure levels of 16,000 mRNA species in solution

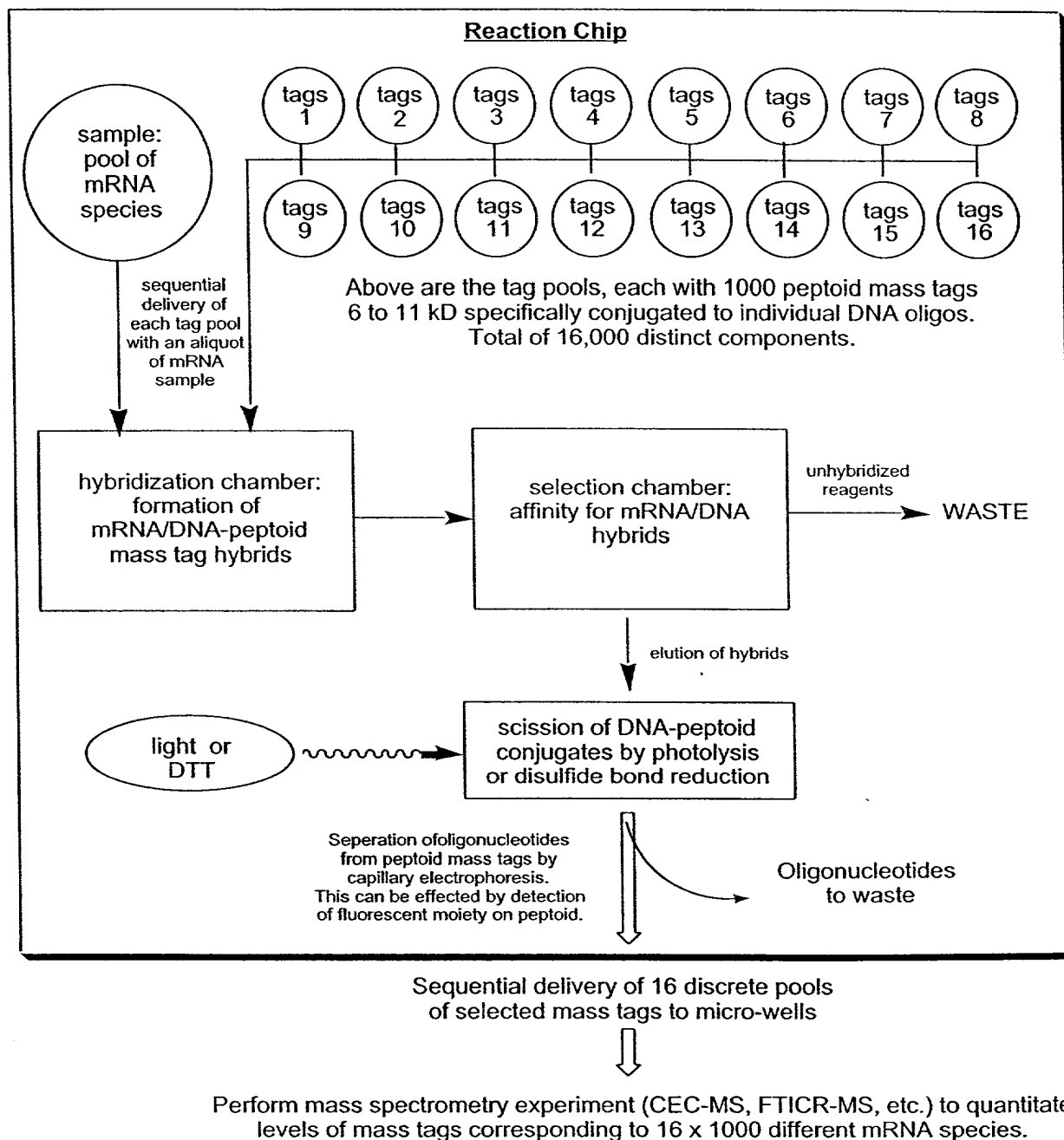


FIGURE 20

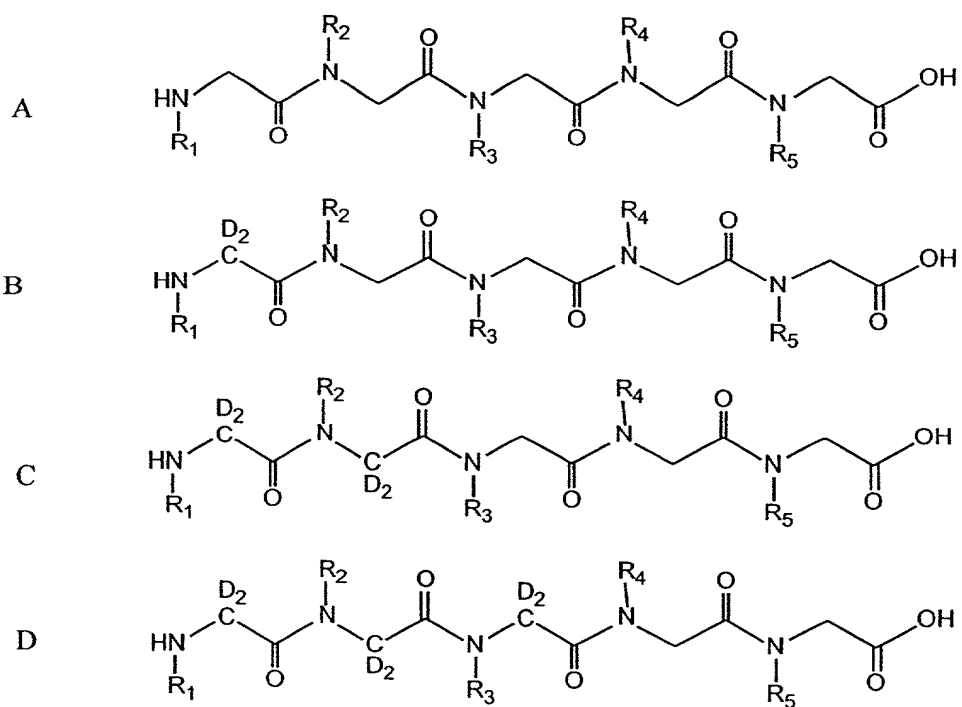


FIGURE 21

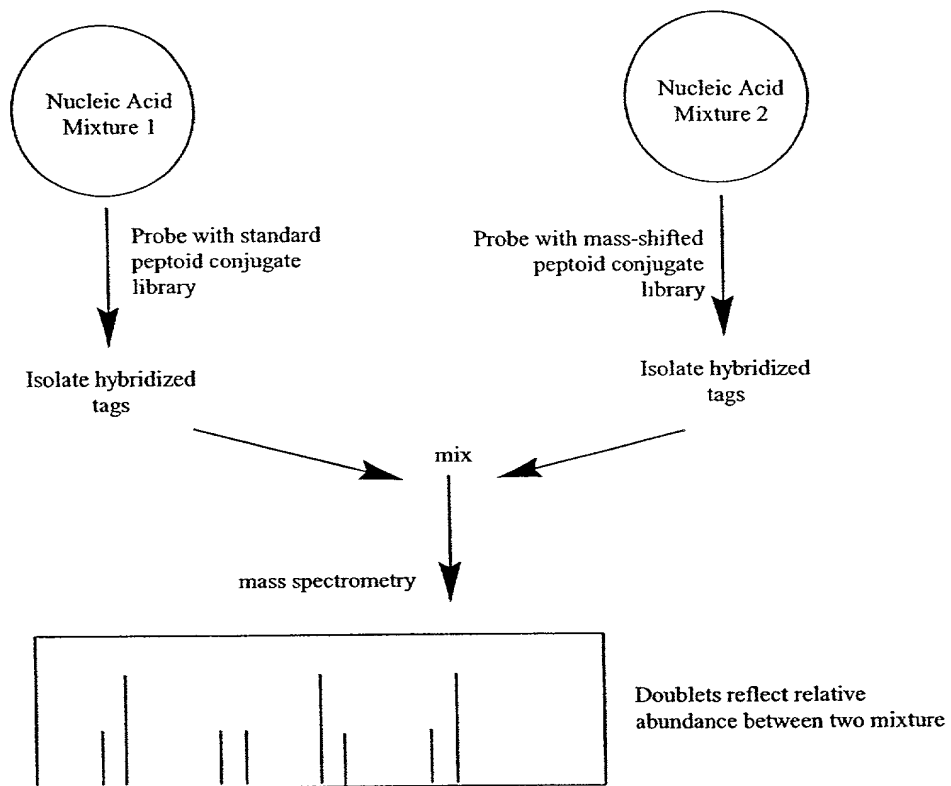


FIGURE 22

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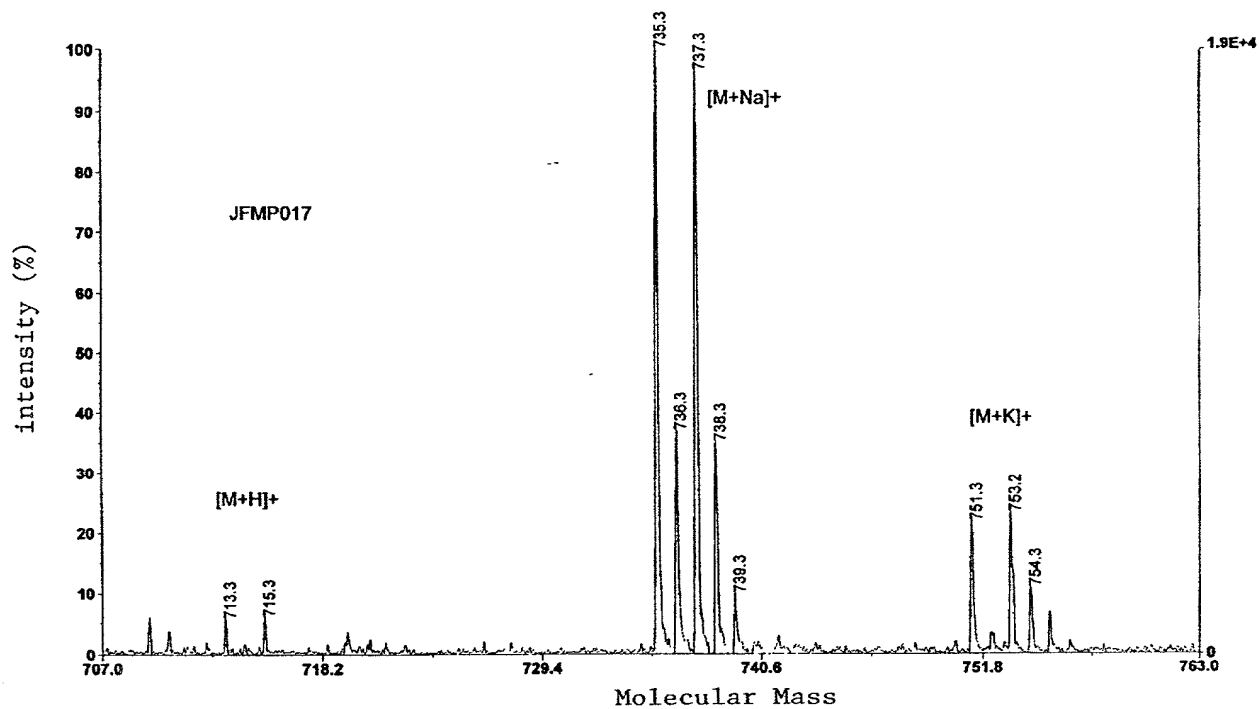


FIGURE 23